American Journal of Medical Genetics 92:157 (2000)

Letter to the Editor

Craniosynostosis: Molecular Testing—A Necessity for Counseling

To the Editor:

We wish to underscore Dr. Andrew Wilkie's comments [Wilkie, 2000] and we are in disagreement with the authors' reply to him [Bower et al., 2000]. Wilkie agrees with Singer et al. [1999] on the need to ensure that families with craniosynostosis are offered genetic counseling and cautions against attempting such counseling without the routine use of molecular genetic investigation. In reply to this letter the authors, Bower, Singer, Southall, and Goldblatt, state that "Despite Dr. Wilkie's caution, genetic counseling may need to proceed without the use of molecular genetic investigation. Such investigation is not available in all centers and may not alter clinical management even if it is."

Clinical management, in addition to surgical intervention and supportive care, should include recurrence risk counseling for the index case and other relatives. In our series of consecutive patients with nonsyndromic unicoronal synostosis, 11% (4/37) were found to have the P250R mutation in FGFR3 [Gripp et al., 1998]. We were unable to distinguish these cases from those without the mutation (based on their physical findings). Similarly, Lajeunie et al. [1999] found an incidence of 7% (2/27) of patients with unicoronal synostosis to carry the FGFR3 mutation. Thus, for appropriate clinical management these individuals need to be identified through mutation testing and counseled regarding the 50% recurrence risk to their offspring.

Once a mutation has been identified in a patient, parental studies need to be performed in order to define their recurrence risk. Physical examination has not proven to be adequate to distinguish mutation carriers. In the series of Lajeunie et al., ten individuals who carried the mutation had no clinical or radiographical evidence of craniosynostosis. At the time of publication of our series [Gripp et al., 1998] three of four sets of parents of affected propositi were available for mutational analysis. The three fathers were identified as mutation carriers, none of whom had come to prior medical attention. One had subtle downslant of palpebral fissures and macrocephaly; one had macrocephaly only; and the third had no abnormal physical findings. The fourth father was initially lost to follow-up; he has subsequently had another affected child and has now been tested and found to carry the mutation. He is clinically normal.

In summary, there are circumstances where clinical management necessitates molecular testing in order to determine recurrence risk since physical examination is not adequate to identify mutation carriers.

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Received 7 January 2000; Accepted 7 January 2000